IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

GALDERMA LABORATORIES, L.P. and NESTLÉ SKIN HEALTH S.A., Plaintiffs, v. ACTAVIS LABORATORIES UT, INC., Defendant.	C.A. No.: 15-232 (LPS)

DECLARATION OF RICHARD L. GALLO, M.D., Ph.D.

I, Richard L. Gallo, M.D., Ph.D., hereby declare the following:

1. At the request of counsel for Actavis Laboratories UT, Inc., ("Actavis"), I hereby submit this expert declaration in support of Actavis' Opening Claim Construction brief.

2. I have been informed that Actavis has filed an Abbreviated New Drug Application ("ANDA") seeking approval from the U.S. Food and Drug Administration ("FDA") to market 0.33% brimonidine topical gel labeled for topical treatment of persistent (nontransient) facial erythema of rosacea.

3. I have been informed that, based on Actavis' ANDA filing, Plaintiffs Galderma Laboratories, L.P. ("Galderma") and Nestlé Skin Health S.A. ("NSH) (collectively, "Plaintiffs") have asserted infringement of claim 1 of U.S. Patent No. 7,439,241 ("the '241 patent") (Ex. 1[1]), claims 1-3 of U.S. Patent No. 8,426,410 ("the '410 patent") (Ex. 2), claims 1-4 of U.S. Patent No. 8,859,551 ("the '551 patent) (Ex. 3), claims 1, 2, 4, 6 and 11-13 of U.S. Patent No.

[1] The Exhibits referenced in this section describing the patents-in-suit refer to the Exhibits in the parties' Joint Appendix (D.I. 64).

8,410,102 (“the ’102 patent”) (Ex. 6), claims 1, 2, 4-11, and 13-23 of U.S. Patent No. 8,513,247 (“the ’247 patent”) (Ex. 4), and claims 1, 2, 4-10, and 12-22 of U.S. Patent No. 8,513,249 (“the ’249 patent”) (Ex. 5) (collectively “patents-in-suit”) against Actavis.

4. In reaching my opinions, I have relied on, *inter alia*, my expertise, the patents-in-suit, selections from the prosecution histories of the patents-in-suit, the parties’ proposed claim constructions, and related documents. It is my understanding that fact discovery is ongoing, and expert discovery has not yet begun. I reserve the right to supplement or amend this declaration, as well as to submit additional declarations if asked to do so.

Qualifications

5. My qualifications and credentials are set forth in my curriculum vitae, attached hereto as Exhibit A. A brief overview of my qualifications is set forth below.

6. I received a Bachelor’s degree from the University of Chicago in 1980. I then received a M.S. in toxicology from University of Rochester in 1983. Following that, I received a Ph.D. in Radiation Biology, Biophysics and Toxicology from University of Rochester and an M.D. from University of Rochester School of Medicine, both in 1986. Following receipt of my M.D. and Ph.D., I was a resident in Pediatrics at Johns Hopkins Hospital from 1986-1987. I was next a resident in Dermatology at Harvard Medical School from 1987-1991. I then completed a Postdoctoral Fellowship at Harvard Medical School from 1991-1995.

7. I am currently Professor of Dermatology, the Interim Chair of the Department of Dermatology, and a Member of the BioMedical Sciences Graduate Program at University of California, San Diego. I am also the Section Chief in Dermatology in the VA San Diego Healthcare System, and have been since 1999.

8. At UCSD, my first position was as Associate Professor IR of Medicine and Pediatrics from 1999-2005, and then Professor of Medicine (Dermatology) and Pediatrics from 2005-2015. Prior to my time at UCSD, I held several positions at Harvard Medical School, including Research Fellow in Dermatology from 1987-1991, Instructor in Dermatology from 1991-1995, and Assistant Professor of Dermatology from 1995-1999. From 1986-1987, I was also an Instructor in Pediatrics at Johns Hopkins University.

9. During my career, I have served in various leadership roles and on several committees, including as President of the National Association of VA Dermatologists, the Board of Directors of the Association of Professors of Dermatology, Rosacea Council of the American Academy of Dermatology, and the Board of Directors of the Society of Investigative Dermatology. I currently am the assistant Secretary-Treasurer of the Society for Investigative Dermatology and am on the Scientific Advisory Committee for the National Eczema Association, the Scientific Advisory Board for the American Skin Association, and the Scientific Advisory Board for the National Rosacea Society.

10. I have served as a reviewer for a number of scientific journals, including Nature, Nature Medicine, Science, Journal of Investigative Dermatology, Journal of the American Academy of Dermatology, Pediatric Dermatology, Lancet, Experimental Dermatology, and others. I currently am on the Editorial Boards for the Journal of Dermatological Science, the European Journal of Dermatology, and The Journal of Biological Chemistry. I am also currently an Associate Editor of the Journal of Investigative Dermatology.

11. I am board certified by the American Academy of Dermatology. I am also a member of the Society for Investigative Dermatology, American Academy of Dermatology, the

American Dermatology Association, the Association of Professors of Dermatology, and an Honorary Member of the Japanese Dermatology Society.

12. My research has sought to uncover basic mechanisms of skin immune defense. My research has also sought to look into the underlying mechanisms and molecular pathology of rosacea, and the role that the immune system plays in the disorder. I have received numerous grants from a number of public and private entities to conduct research, including from the National Rosacea Society.

13. I have been invited to present numerous lectures to hospitals, universities, and professional meetings in the field of dermatology, microbiology, immunology and cell biology, including lectures describing my own research. In addition, I have authored over 250 peer-reviewed publications, books, reviews, chapters, and editorials generally relating to dermatology, including numerous articles on rosacea.

Prior testimony

14. Within the preceding four years, I have not testified at trial or testified by deposition in any legal cases.

Compensation

15. I am being compensated for my time spent working on this case at my regular consulting rate of $750.00 per hour. My compensation is not dependent upon the substance of my opinions or the outcome of this case.

Level of ordinary skill in the art

16. I have been informed that in assessing the validity or infringement of a U.S. patent, the Court must first construe or interpret the asserted claims of the patent. I understand that as part of the claim construction process, the Court must determine the level of ordinary skill

in the art at the time of the alleged invention of the asserted claims. When discussing the ’241 and ’410 patents, I am referring to the level of skill of a person of ordinary skill in the art as of May 2003 (the filing date of the earliest application to which the ’241 and ’410 patents claim priority) and when discussing the ‘247 and ‘249 patents, I am referring to the level of skill of a person of ordinary skill in the art as of March 2010 (the filing date of the earliest application to which the ’247 and ’249 patents claim priority). I have further been informed that to determine the appropriate level of skill in the art, one considers several factors, including: the types of problems encountered in the art; prior art solutions to those problems; the rapidity with which innovations are made; the sophistication of the technology; and the educational level of active workers in the field at the time of the alleged invention. I also have been informed that a person of ordinary skill in the art is a person capable of devising routine solutions to routine problems when such problems present themselves.

17. It is my opinion that a person of ordinary skill in the art of the patents-in-suit would be an M.D., or hold a Ph.D. in pharmacology, pharmaceutical sciences, pharmacy or a related field, with at least two years’ experience in conducting research in the field of dermatology, vascular function, and/or drug development of topical formulations, it being understood that the emphasis of expertise may vary for the different claims of the patents-in-suit. Alternatively, the person of ordinary skill could possess a B.S. or an M.S. in pharmacology, pharmaceutical sciences, pharmacy or a related field, with at least five years’ experience (in the case of a B.S.) or at least three years’ experience (in the case of an M.S.) in conducting research in the field of dermatology, vascular function, and/or drug development of topical formulations, it being understood that the emphasis of expertise may vary for the different claims of the patents-in-suit.

Background on Rosacea

18. Well before May 2003, rosacea was a widely recognized dermatological skin disorder with a well-defined variety of symptoms. Some symptoms of rosacea include facial redness, telangiectasia, papules and pustules, and thickening skin and enlargement of the nose (rhinophyma). The facial redness is one of the more common primary features of rosacea, and often manifests as blushing or flushing (transient erythema) or as persistent redness (persistent or nontransient erythema).

Summary of Opinion

19. I have been asked to provide my opinion on how a person of ordinary skill in the art would have understood the claim terms "[treating rosacea and] the symptoms associated therewith," "redness associated with rosacea," and "pharmaceutical composition." It is my opinion that a person of ordinary skill in the art would have understood "[treating rosacea and] the symptoms associated therewith" in the context of the '410 patent to mean "treating rosacea and symptoms including frequent blushing, frequent irritation of the facial skin, erythema, telangiectasia, papules, pustules, and rhinophyma." A person of ordinary skill in the art would not agree with Plaintiffs' proposed construction ("treating rosacea or at least one discernable symptom thereof").

20. I have been asked how a person of ordinary skill in the art would have understood the phrase "redness associated with rosacea" in the context of the '241 patent. It is my opinion that a person of ordinary skill in the art would have understood that term to mean "redness related to that observed in rosacea." A person of ordinary skill in the art would not agree with Plaintiffs' proposed construction ("redness (erythema) due to rosacea").

21. I have been asked how a person of ordinary skill in the art would have understood the phrase "pharmaceutical composition" in the context of the '241 patent. It is my opinion that a person of ordinary skill in the art would have understood that term to mean "a composition comprising a pharmaceutical compound and a pharmaceutically acceptable carrier."

22. I also have been asked to provide my opinion on how a person of ordinary skill in the art would have understood the phrases listed in Exhibit B, which are used in the asserted claims of the patents-in-suit. That is, I have been asked to consider whether those terms would alter the way that one performs the method set forth in the asserted claims or the formulation of the claimed compositions. It is my opinion that they would not; rather, a person of ordinary skill in the art would have understood those terms simply to be statements of intended or desired effects or results of the therapy—not limitations on how the drug is administered or how the compositions are formulated.

[Treating Rosacea and] the Symptoms Associated Therewith

23. I have been asked to provide my opinion on how a person of ordinary skill in the art would have understood the phrase "[treating rosacea and] the symptoms associated therewith" in claim 1 of the '410 patent. In my opinion, the claim language is clear as written: the claimed method requires treating rosacea itself (the underlying disorder) and the symptoms associated therewith. A person of ordinary skill in the art at the relevant time would have known that the symptoms associated with rosacea include frequent blushing, frequent irritation of the facial skin, erythema, telangiectasia, papules, pustules, and rhinophyma.

24. Actavis' proposed construction is supported by the specification of the '410 patent. For example, the '410 patent distinguishes the previously known treatments which largely treated only certain symptoms, and notes that these previous treatments did not treat all

symptoms of rosacea or the disease itself. ’410 pat. at 1:66-67, 2:12-15, 2:18-22, 2:25-27. The ’410 patent states “there remains a need for topical formulations for treatment of inflammatory skin disorders like rosacea and its symptoms.” ’410 patent at 2:30-31. Based on this similar language to the claimed “rosacea and the symptoms associated therewith,” a person of ordinary skill in the art would have understood that the claimed treatment was intended to fill the need for a treatment of the disease itself and all symptoms associated therewith.

Redness Associated with Rosacea

25. I have next been asked to provide my opinion on how a person of ordinary skill in the art would have understood the claim term “reducing redness associated with rosacea” in claim 1 of the ’241 patent. ’241 pat. 24:31. It is my opinion that a person of ordinary skill in the art would have understood this term to mean “redness related to that observed in rosacea.” I disagree with Plaintiffs’ construction limiting this term to “redness ‘due to’ rosacea.”

26. Actavis’ proposed construction, where “associated with” is recognized as the broad term meaning related to, is supported by the specification of the ’241 patent. For example, the only use of the phrase “associated with rosacea” in the patent simply states that “erythema associated with rosacea is caused by dilation of the superficial vasculature of the face.” ’241 patent at 1:51-55. Not all erythema caused by such dilatation is due to rosacea. Example 13 provides an example of such erythema related to that observed in rosacea, but not “due to” rosacea. In Example 13, vasodilation was induced with the compound methyl nicotinate. The resulting redness was reduced or prevented by pre-application of brimonidine or another α adrenoceptor agonist. As such, a person of ordinary skill in the art would have understood the claimed term “redness associated with rosacea” encompasses “redness related to that observed in rosacea” that is not necessarily “due to” rosacea.

Pharmaceutical Composition

27. I have next been asked to provide my opinion on how a person of ordinary skill in the art would have understood the claim term of "pharmaceutical composition" in the phrase "…topically administering a pharmaceutical composition comprising an effective amount of brimonidine or a pharmaceutically acceptable salt thereof…" in claim 1 of the '241 patent. It is my opinion that a person of ordinary skill in the art would have understood a pharmaceutical composition in the context of the '241 patent to mean "a composition comprising a pharmaceutical compound and a pharmaceutically acceptable carrier." To a person of ordinary skill in the art, the term "pharmaceutical composition" generally is understood to refer to a formulation that includes at least one pharmaceutically acceptable carrier (*e.g.*, a solvent or other excipient) that is used to formulate and deliver the active pharmaceutical ingredient.

28. The sole claim of the '241 patent requires that the pharmaceutical composition be "topically administer[ed]" to "the skin of a patient." Accordingly, a person of ordinary skill in the art would understand the pharmaceutical composition of claim 1 to be a topical formulation. The term "topical formulation" is explicitly defined in the patent to include "a pharmaceutically acceptable topical carrier." '241 patent at 10:16-18. A person of ordinary skill in the art, therefore, would understand the term "pharmaceutical composition" to include a pharmaceutically acceptable carrier.

The claims of the patents-in-suit contain statements of intended effects that do not affect how the drug is administered or how the compositions are formulated.

29. I have reviewed the claim terms set forth in Exhibit B, which appear in certain asserted claims of the patents-in-suit, and carefully considered whether recitation of those terms will alter the way in which a medical practitioner or patient will prescribe or perform the claimed methods or prescribe or use the claimed compositions. They do not. Rather, it is my opinion that

the claim phrases set forth in Exhibit B are merely a list of intended effects, or desired outcomes, following the administration of brimondine according to the claimed methods or following topical application of the claimed compositions.

30. I have been informed that dependent claims incorporate the limitations of the independent claims from which they depend. As such, claim 3 of the ’410 patent recites a method of “topically administering [a composition] to the skin of a patient” “wherein the composition acts locally in the skin of the patient.”[2]

31. It is my opinion that the phrase “acts locally in the skin of the patient” is simply a consequence of topical administration. This phrase does not alter the way in which the claimed method is performed.

32. The patent specification explains that it is the “topical skin composition that insures that the compounds are effective in the skin of the patient but do not penetrate the skin in sufficient amounts to induce serious systemic side effects.” *See* ’410 patent at 3:27-30. In other words, “topically administering to the skin of a patient in need of such treatment a composition” as described in claim 1 would insure that the “composition acts locally in the skin of the patient.” A person of ordinary skill in the art would have understood the latter phrase is redundant.

33. Several claims of the ’247 and ’249 patents include clauses that state the “success profiles” resulting from the performance of the claimed methods or the administration of the claimed compositions. Certain claims of the ’249 patent also include clauses that state the pharmacokinetic profiles achieved by the performance of the claimed methods or administration of the claimed compositions. It is my opinion that these clauses do not reflect requirements in

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[2] This recitation of the language of claim 3 incorporates the language from independent claim 1 upon which claim 3 depends.

performing the claimed methods or formulating the claimed compositions. Rather, these phrases recite the expected and hoped-for consequences of performing the methods or administering the compositions as otherwise claimed.

34. The patent specifications discuss how use of the claimed concentration range of brimonidine (0.4% to 0.6% (w/w)), causes the "result" or "effect" of achieving the claimed success and pharmacokinetic profiles. *See* '247 patent at 13:1-5, 5:53-55, 6:23-35, 6:49-55. In other words "topically administering to a skin area affected by the erythema or the symptom a topical composition comprising, relative to the total weight of the composition, 0.4% to 0.6% by weight of brimonidine and a pharmaceutically acceptable carrier" would naturally result in the claimed clinical and pharmacokinetic profiles.

35. The intended "success profiles" set forth in the claim terms listed in Exhibit B may not be observed in every patient. Indeed, controlled clinical studies reported in the medical literature indicate that, while a statistically significant percentage of patients experience an improvement in nontransient erythema after treatment with 0.5% brimonidine tartrate relative to those treated with placebo, some patients' responses do not significantly differ from those treated with placebo. However, the method of administration set forth in the claims is not altered to achieve the intended effect. A physician cannot determine in advance whether a patient suffering from nontransient erythema of rosacea will show improvement through the administration of the claimed composition. Therefore the patient is instructed to self-administer the same formulation of 0.5% brimonidine tartrate irrespective of the desired outcome.

36. I declare under penalty of perjury that the foregoing is true and correct to the best of my knowledge and belief.

Date: 3/22/16

Richard L. Gallo, M.D., Ph.D.